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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/719,480	11/21/2003	David Y. Zhang	251305/0040 SBP:KYH:AEW	3654

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EXAMINER	
LU, FRANK WEI MIN	
ART UNIT	**PAPER NUMBER**
1634	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/05/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/719,480	ZHANG ET AL.	
	Examiner	Art Unit	
	Frank W. Lu	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 October 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-55* is/are pending in the application.

4a) Of the above claim(s) *See Continuation Sheet* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,8,9,13-15,18,19,23-25,28,29,33-35,38,39 and 43-45* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *21 November 2003* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Continuation of Disposition of Claims: Claims withdrawn from consideration are 6,7,10-12,16,17,20-22,26,27,30-32,36,37,40-42 and 46-55.

DETAILED ACTION

Election/Restrictions

1. Applicant's election of Group I, claims 1-9, 13-19, 23-29, 33-39, and 43-45 and species (1) (claims 5, 15, 25, and 35) and (7) (claims 8, 9, 18, 19, 28, 29, 38, and 39) with traverse in the reply filed on October 11, 2006 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Therefore, claims 1-5, 8, 9, 13-15, 18, 19, 23-25, 28, 29, 33-35, 38, 39, and 43-45 will be examined.

Drawings

2. Some bands in Figure 18 are not visible. Please replace Figure 18 in response to this office action.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1-5, 8, 9, 13-15, 18, 19, 23-25, 28, 29, 33-35, 38, 39, and 43-45 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for amplifying a circular oligonucleotide using the methods recited in claims 1-5, 8, 9, 13-15, 18, 19, 23-25, 28, 29, 33-35, 38, 39, and 43-45, does not reasonably provide enablement for detecting a target nucleic acid in a sample using the methods recited in claims 1-5, 8, 9, 13-15, 18, 19, 23-25, 28,

29, 33-35, 38, 39, and 43-45. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

In *In re Wands*, 858 F.2d 731,737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) the court considered the issue of enablement in molecular biology. The Court summarized eight factors to be considered in a determination of "undue experimentation". These factors include: (a) the quantity of experimentation necessary; (b) the amount of direction or guidance presented; (c) the presence or absence of working examples; (d) the nature of the invention; (e) the state of the prior art; (f) the relative skill of those in the art; (g) the predictability of the art; and (h) the breadth of the claims. The Court also stated that although the level of skill in molecular biology is high, results of experiments in molecular biology are unpredictable.

To begin, there is no direction or guidance in the specification to show that the methods recited in claims 1-5, 8, 9, 13-15, 18, 19, 23-25, 28, 29, 33-35, 38, 39, and 43-45 can be used for detecting a target nucleic acid in a sample. While the relative skill in the art is very high (the Ph.D. degree with laboratory experience), there is no predictability whether the methods recited in claims 1-5, 8, 9, 13-15, 18, 19, 23-25, 28, 29, 33-35, 38, 39, and 43-45 can be used for detecting a target nucleic acid in a sample.

Claims 1-5, 8, 9, 13-15, 18, 19, 23-25, 28, 29, 33-35, 38, 39, and 43-45 are directed to a method for detecting a target nucleic acid in a sample. First, although steps (b) and (c) of claim 1 require that at least one forward primer comprises a sequence complementary to a portion of the circular oligonucleotide probe and an oligonucleotide primer pair comprises a first primer comprising a first sequence that is substantially identical to a portion of the circular

oligonucleotide probe, since claim 1 does not indicate that the at least one forward primer comprising a sequence is complementary to which portion of the circular oligonucleotide probe and the first primer of the oligonucleotide primer pair comprising a first sequence is substantially identical to which portion of the circular oligonucleotide probe, and does not require that the second primer of the oligonucleotide primer pair is complementary to the circular oligonucleotide probe, it is unclear whether the product amplified from the circular oligonucleotide probe contains a nucleotide sequence that is complementary to the first or second primer of the oligonucleotide primer pair. If the product amplified from the circular oligonucleotide probe does not contain a nucleotide sequence that is complementary to the first or second primer of the oligonucleotide primer pair, the oligonucleotide primer pair cannot be used as primers for amplifying the circular oligonucleotide probe so that detection of a signal in step (f) of claim 1 cannot indicate the presence of the target nucleic acid in the sample. Second, although step a) of claim 13 or 23 requires contacting the target nucleic acid with a circular oligonucleotide probe under conditions that allow hybridization between complementary sequences in the target nucleic acid and the circular oligonucleotide probe, since claim 13 or 23 does not require that the target nucleic acid is fully complementary to the circular oligonucleotide probe and the polymerase is a polymerase which lacks 3' to 5' exonuclease activity, when the polymerase is a polymerase which has 3' to 5' exonuclease activity, it is possible that the target nucleic acid is cleaved due to 3' to 5' exonuclease activity of the polymerase so that detection of a signal in step (e) of claim 13 or 23 cannot indicate the presence of the target nucleic acid in the sample. Third, although steps (b) and (c) of claim 33 require that at least one forward primer comprises a sequence complementary to a portion of the

circular oligonucleotide probe and multiple oligonucleotide primers comprises a first primer comprising a first sequence that is substantially identical to a portion of the circular oligonucleotide probe, since claim 33 does not indicate that the at least one forward primer comprising a sequence is complementary to which portion of the circular oligonucleotide probe and the first primer comprising a first sequence is substantially identical to which portion of the circular oligonucleotide probe, and does not require that the second primer or third primer of the multiple oligonucleotide primers is complementary to the circular oligonucleotide probe, it is unclear whether the product amplified from the circular oligonucleotide probe contains a nucleotide sequence that is complementary to the first or second or third primer of the multiple oligonucleotide primers. If the product amplified from the circular oligonucleotide probe does not contain a nucleotide sequence that is complementary to the first or second or third primer of multiple oligonucleotide primers, the first, second and third primers cannot be used as primers for amplifying the circular oligonucleotide probe so that detection of a signal in step (e) of claim 33 cannot indicate the presence of the target nucleic acid in the sample. Fourth, although steps (a) to (c) of claim 43 indicate that at least one forward primer comprises a sequence complementary to a portion of the circular oligonucleotide probe, an oligonucleotide primer pair comprises a first primer comprising a first sequence that is substantially identical to a portion of the circular oligonucleotide probe and at least one reverse primer comprising a sequence is substantially identical to a portion of the circular oligonucleotide probe, since claim 43 does not require that the at least one forward primer comprising a sequence is complementary to which portion of the circular oligonucleotide probe, the first primer of the oligonucleotide primer pair comprising a first sequence is substantially identical to which portion of the circular

oligonucleotide probe, the at least one reverse primer comprising a sequence is substantially identical to which portion of the circular oligonucleotide probe, and does not require that the second primer of the oligonucleotide primer pair or the at least one reverse primer is complementary to the circular oligonucleotide probe, it is unclear whether the product amplified from the circular oligonucleotide probe contains a nucleotide sequence that is complementary to the first or second primer of the oligonucleotide primer pair or the at least one reverse primer. If the product amplified from the circular oligonucleotide probe does not contain a nucleotide sequence that is complementary to the first or second primer of the oligonucleotide primer pair or the at least one reverse primer, the oligonucleotide primer pair cannot be used as primers for amplifying the circular oligonucleotide probe so that detection of a signal in claim 45 cannot indicate the presence of the target nucleic acid in the sample. In view of claims 1-5, 8, 9, 13-15, 18, 19, 23-25, 28, 29, 33-35, 38, 39, and 43-45, it is unclear how to detect a target nucleic acid in a sample using the methods recited in claims 1-5, 8, 9, 13-15, 18, 19, 23-25, 28, 29, 33-35, 38, 39, and 43-45.

With above unpredictable factor, the skilled artisan will have no way to predict the experimental results. Accordingly, it is concluded that undue experimentation is required to make the invention as it is claimed. The undue experimentation at least includes to test whether the methods recited in claims 1-5, 8, 9, 13-15, 18, 19, 23-25, 28, 29, 33-35, 38, 39, and 43-45 can be used for detecting a target nucleic acid in a sample.

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 1-5, 8, 9, 13-15, 18, 19, 23-25, 28, 29, 33-35, 38, 39, and 43-45 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

7. Claim 1 or 43 is rejected as vague and indefinite. Since claim 1 or 43 does not require that the first primer or the second primer or the reversed primer is complementary to a fully complementary strand of the circular nucleic acid sequence, it is unclear whether the first primer, the second primer and the reversed primer is required for the claimed method. Please clarify.

8. Claim 13 is rejected as vague and indefinite. Since claim 13 does not require that the first primer or the second primer of the second oligonucleotide primer pair is complementary to a fully complementary strand of the circular nucleic acid sequence, it is unclear whether the first primer and the second primer of the second oligonucleotide primer pair are required for the claimed method. Please clarify.

9. Claim 23 is rejected as vague and indefinite. Since claim 1 or 43 does not require that the reversed primer is complementary to a fully complementary strand of the circular nucleic acid sequence, it is unclear whether the reversed primer is required for the claimed method. Please clarify.

10. Claim 23 or 33 is rejected as vague and indefinite because it is unclear what means "at least one multiple oligonucleotide primer comprising a first primer, a second primer and a third primer" because one multiple oligonucleotide primer cannot comprise a first primer, a second primer and a third primer. Please clarify.

11. Claim 33 is rejected as vague and indefinite. Since claim 33 does not require that the first primer or the second primer or third primer of multiple oligonucleotide primers is

complementary to a fully complementary strand of the circular nucleic acid sequence, it is unclear whether the first primer, the second primer, and third primer are required for the claimed method. Please clarify.

12. Claim 43 recites the limitation "the circular oligonucleotide probe" in step (c) of the claim. There is insufficient antecedent basis for this limitation in the claim because there is no phrase "circular oligonucleotide probe" in steps a) and b) of the claim. Please clarify.

Conclusion

13. No claim is allowed.

14. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CAR § 1.6(d)). The CM Fax Center number is (571)273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frank Lu, Ph.D., whose telephone number is (571)272-0746. The examiner can normally be reached on Monday-Friday from 9 A.M. to 5 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla, can be reached on (571)272-0735.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

December 22, 2006

FRANK LU
PRIMARY EXAMINER